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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,130	09/21/2000	John W. Barnwell	5986/17686-US5	8596

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/667,130	BARNWELL, JOHN W.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *attachment*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The response filed September 26, 2003 has been entered into the record. Claims 22 and 23 are pending and under examination, all other claims having been canceled.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Maintained

The preliminary amendment filed 9-21-00 stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: " EcoRI digest of purified ..... for 2 months." which is inserted at page 5, line 18 after "1989". The objection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02 and the last office action of record.

Applicant's arguments have again been considered but are again not persuasive. Applicant argues Dr. Crothers declaration that opines that the conditions specifically disclosed in the Southern et al article would be considered "stringent". This is not persuasive again, the incorporation by reference must be specific. Declarant is basically attesting that any condition of hybridization is stringent. This is not persuasive, Southern et al does not define these conditions as "Stringent". Further, Southern et al is a guidebook to selection of general hybridization conditions and does not define any specific conditions as stringent. The specification does not direct one to any specific conditions set forth in Southern et al and erroneously indicates that Southern et al defines stringent hybridization conditions, it does not. The incorporation of the specific material inserted into the specification is not a result of a specific incorporation by reference by pointing in

particular to the relied upon teachings in Southern et al, but instead reflects an improper general incorporation by reference to any condition recited therein. Nowhere in Southern et al is the word "Stringent" used. Therefore, nothing in Southern et al teaches "stringent conditions" as specifically referenced by the specification. As such, the skilled artisan would not be pointed to any particular hybridization conditions recited by Southern et al, none are characterized by Southern et al as "stringent" as opposed to not stringent. As previously indicated, Southern et al is merely a guidebook for selection of conditions that allow for hybridization between two nucleic acids and these conditions are dependent on the particular structure (G+C) content of the nucleic acid under study. As such, there is nothing articulated in the specification to any particular set of conditions in Southern et al. The declaration of Dr. Crothers is not persuasive on this point, *it is the specification that must particularly point to those conditions which are considered incorporated by reference.* This point is made completely clear in the office actions of record. Applicant argues that Dr. Crothers' conclusion with regard to experimentation conditions is based upon his examination of the experimental conditions explored and used in the Southern et al publication. This again is not persuasive, Dr. Crothers' opinion is not supported by extrinsic evidence for the recited nucleic acid and moreover supports the assertion of the examiner that the incorporation by reference is not specific to any subject material in Southern et al. This argument appears to support that the reference is an improper general incorporation and does not in fact specifically reference the incorporated material as required by the MPEP and Hawkins decisions as previously set forth in the all the office actions of record. Unlike *In re Voss* , the incorporation is not reasonably precise, it was not made for clarity and appears erroneous on its face. It specifically references the Southern et al "as defined by", but the reference did not define such conditions, but recites multiple conditions. This application is unlike the situation in *In re Voss*, because in Voss, Applicant pointed to a the relied upon material "discussion of glass-ceramic material and their production". The incorporation by reference in this specification does not. The

entirety of Southern et al is drawn to selection of hybridization conditions and the variation of those to achieve specific hybridization. There is no discussion of stringency and no particular conditions referenced that are particularly defined as such. It is the specification that must clearly and unambiguously point to the incorporating material. Unlike the relied upon paragraph in *In re Voss*, that does such, this specification does not for all the previous reasons made of record. Applicant argues that stringent conditions are not empirical in nature and are in fact a combination of temperature and salt conditions. Applicant argues that the concept of stringency (i.e. the intrinsic specificity of the hybridization reaction depends on the annealing conditions employed was familiar to those of ordinary skill in the field. While this may be true, the concept of "stringency" does not define any particular conditions, it is *relative*. Kennel et al "Principles and properties of nucleic acid hybridization", Progr. Nucl. Acid Res. Mol. Biol. 11:259-301, 1971) teaches that ". It should be emphasized that the extent to which mismatched hybrids can form is relative and dependent upon the "stringency" of the reaction conditions. The stringency refers to the extent to which the reaction conditions allow only completely complementary structures to form. Generally, stringency is proportional to temperature and inversely proportional to salt conditions." (page 293, first full paragraph). Thus, stringent conditions are not a particular set of defined conditions because stringency is a relative concept and "stringent conditions" can vary depending upon the temperature and salt conditions. The skilled artisan would not pick one set of conditions over any other set in view of the teachings of Southern et al because the specification does not teach nor does it contemplate the degree of mismatch contemplated. As such, this specification does not point to any particular conditions that it defines or Southern et al defines as "stringent". In contrast to Applicants assertions, the Southern et al reference uses multiple conditions of temperature in salt (see figures) and as such does not define any particular conditions. There are no one set of conditions that are "defined as stringent conditions". Even if one were to consider all the conditions set forth in Southern et al. as

"stringent", then Applicant's incorporation by reference falls to the level of a improper general incorporation by reference. Applicant argues that as evidence that "stringent hybridization conditions" are not empirical in nature and need not be independently determined for every different nucleic acid, Applicants point to the Written description guidelines Example 9. This is not persuasive, it is relying upon hypothetical teachings. All of the Examples are hypothetical in nature. Declarant and Kennel's asserted concept of stringency emphasizes the relative nature of "stringency" and that no particular conditions are art defined as stringent, nor does Southern et al define such. As to the nature of empirical nature of hybridization, the property of G+C content on Tm etc are all exemplified by Kennel as cited *supra*. The structure of the nucleic acids completely reflects its ability to form a complex with a target under specifically defined conditions. However, this specification does not reference with any particularity any specifically defined conditions. It relies upon an vague incorporation by reference utilizing language not present in the reference and the skilled artisan is left guess as to the meaning thereof and the particular conditions referenced. Declarant's opinion is not persuasive on this issue because it essentially states that all hybridization conditions are stringent, while the art defines stringency as a relative concept and not defined by any particular art defined conditions.

The rejection is maintained for reasons made of record herein and all the previous reasons made of record.

Claims 22 and 23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 26 and 28 of copending Application No. 08/719,821, now US Patent No. 6,706,872. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of full complements claimed in the copending application, would by definition hybridize to SEQ ID NO:1 and thus anticipate the instant genus claims . The

rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02. Applicants indicate that a terminal disclaimer would be filed upon indication of allowable subject matter. The rejection is hereby maintained until resolution by terminal disclaimer.

Claim 23 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants arguments have been carefully considered but are not persuasive. Applicants argue that the general incorporation by reference of Southern et al that recites numerous hybridization conditions and in view of the Declaration of Dr. Crothers is not persuasive. Applicant's arguments with respect to the insertion of new matter into the specification were not persuasive for reasons set forth above.

Claim 22 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants argue that this is not well taken and should be withdrawn. This is not persuasive for reasons made of record previously and in view of the concept of stringency is relative and that Southern et al does not define any condition that is "stringent". This is not persuasive for reasons made of record previously and Applicant's arguments with respect to the insertion of new matter into the specification were not persuasive for reasons set forth above.

Claims 22 and 23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sigma Molecular biology Product Guide, 1991, pages 54-56). The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants arguments have been carefully considered but are not persuasive. Applicants argue that there is no mention of stringent hybridization conditions in Sigma at all and therefore it can not anticipate the claimed invention. This is not persuasive, the claims are drawn to products by function. Applicants also argue that the rejection is incompatible with the 112, first paragraph rejection of record. This is not persuasive because as Applicants well know, the rejections are made under different statutes that have different specific requirements. The products of the art inherently have the recited function of hybridization based upon their 100% identity across the recited nucleotides. Applicants have not provided any extrinsic evidence that the products of the art would not hybridize under any specific set of allegedly "stringent" conditions.

Since the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the nucleic acid of the prior art does not possess the same functional characteristics of the claimed nucleic acid). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claims 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

Applicants arguments have been carefully considered but are not persuasive. Applicants argue a Declaration by the inventor Dr. Barnwell. Dr. Barnwell attests that SEQ ID NO:2 is in fact the full-length open reading frame and attempts to explain the differences between the apparent molecular weights of the protein as compared with the calculated molecular weight. This is not persuasive, the specification specifically teaches that it is a fragment. This specification the teachings of which are sworn and attested to by Dr. Barnwell. Further, Dr. Barnwell is attesting that they have disclosed the full-length open reading frame of 1011 amino acids and that the sequence of depicted in SEQ ID NO:2 is the complete open reading frame. This is not persuasive on its face. SEQ ID NO:2 is 1018 amino acids in length and is described as a partial sequence. Applicant is arguing that the full length is 1011 amino acids long. This argument is entirely incompatible with the written description of the disclosure. Applicants are attempting to redefine the invention as something that is shorter than that described by SEQ ID NO:2 which is 1018 amino acids long. It is the specification that must teach conception of what is the invention. The specification teaches that the genomic fragment is an incomplete reading frame. Declarant, discovering his error in characterization well after filing this application can not seek to "correct" the specific written description thereof of the specification as filed, by assertion that the nucleic acid of SEQ ID NO:1 is the full-length open reading frame, when the specification clearly indicates otherwise. The declaration of Dr. Barnwell, in essence an attempt to redefine the described invention of the specification after the filing date. The specification does not state that the complete gene codes for 1011 amino acids with a calculated molecular weight of 112,725 Da. There is no recognition of this fact in the specification as filed. Further, one skilled in the art would take the characterization of the gene as incomplete in view of the lack of a recited conventional start codon on the protein, the discrepancy of the molecular weights. Declarant provides many different possible explanations, but no extrinsic evidence that the particular system used provides for a protein having these characteristics. Further, the inability of a

bacterium to splice any introns, would apparently provide for a protein of increased rather than decreased molecular weight because the intervening sequence (introns) would be expressed by the bacterium. Declarant provides no evidence that the this is the case in the described expressed by the method set forth in specification. With respect to in situ proteolysis of the expressed protein, this is hypothetical and does not provide extrinsic evidence that the protein produced by the method described in the specification undergoes *in situ* proteolysis. There is not a single post-translational modification described in the specification with respect to this protein. Therefore, the discrepancy of the molecular weights because of the inability of the bacterium to perform certain post-translational modifications is hypothetical. No posttranslational modifications of the protein encoded by the nucleic acid are taught nor contemplated by this specification. Declarant also attests that discrepancies are common among *Plasmodium* proteins because they contain repeated proline rich amino acid motifs that render them less susceptible to denaturation by SDS. This is not persuasive, there is no evidence to support this problem associated with SEQ ID NO:2. Applicants submit that the instant specification enables the complete open reading frame. Enablement is not the issue here. Written description of the full length open reading frame and whether or not, Applicants at the time of filing, as described by the specification at the time of filing, conveyed possession of the full-length open reading frame. The examiner contends that the written description of the specification did not, convey possession of the full-length open reading frame and as such is not analogous to Example 8. Further, in contrast to Example 8, no asserted function is associated with the protein fragment of SEQ ID NO:2 and coding for a surface protein of *P. vivax* is not a function of the protein, it is not a description of what it does, but where it is located. Location is not equivalent to function of a protein. Applicants were not in possession of the genus comprising SEQ ID NO:1 because they do not describe the full-length open reading frame, nor do they describe the function of the protein. Applicants argues *Wahl Instrument v Acvious Inc.* 950 F2.d 1575 21 USPQ 2d 1123 (Fed Cir. 1991)

indicating that a misrepresentation in a patent specification will only defeat the enablement of an invention if the skilled artisan fails to recognize the mistake and relies on it to practice the invention. This is not persuasive, the question of Wahl involves a best mode inquiry and whether the inventor failed to disclose particular manufacturing procedures beyond the information sufficient for enablement and that such failure gives rise to an inference that he concealed information which one of the ordinary skill in the art would not know. The issue at hand is conception of the full-length open reading frame by way of written description and not concealment of best mode or enablement. Further, the missing descriptive information is not a routine manufacturing choice. For written description of nucleic acids,the nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. This written description inquiry is independent from enablement Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification conveys that the nucleic acid of SEQ ID NO:1 encoding the protein of SEQ ID NO:2 is not the full-length open reading frame. The specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the full length open reading frame as argued, specifically teaches to the contrary and one skilled in the art would not have any specific framework of reference to believe otherwise, since other similar proteins and nucleic acids have not been disclosed in the art. Therefore, unlike Example 8, there is no frame of reference for either completeness of the sequence or function of the protein encoded by the nucleic acid, and the teachings of the specification would necessarily be taken as true. Applicants argue that because there is a single species and reduction to practice of a single species is representative of the genus because one skilled in the art would not expect substantial variation in the sequence. This is not persuasive, as

previously set forth, the claims encompass variants that do not encode proteins. The specification does not disclose that the disclosed species of SEQ ID NO:1 was used in any manner to hybridize to other nucleic acids. Unlike Example 9 of the written description guidelines, there is no disclosed example where SEQ ID NO:1 is used for the isolation of hybridizing nucleic acids. Additionally, the methods of Example 9 used defined conditions and recite a specific functional activity and were demonstrated to have the asserted activity. No such information is provided in this specification, no specific function is disclosed, SEQ ID NO:1 was not used to isolate hybridizing sequences and as such the specie of SEQ ID NO:1 is not representative of a genus of hybridizing sequences with identical biological function. Therefore, the skilled artisan given the written description of the specification would clearly recognize that Applicants had no conception by way of written description of the genus of nucleotides hybridizing under stringent conditions, nor were they in possession, of the full-length open reading frame.

Status of Claims

Claims 22 and 23 stand rejected.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy
Primary Examiner
Art Unit 1645